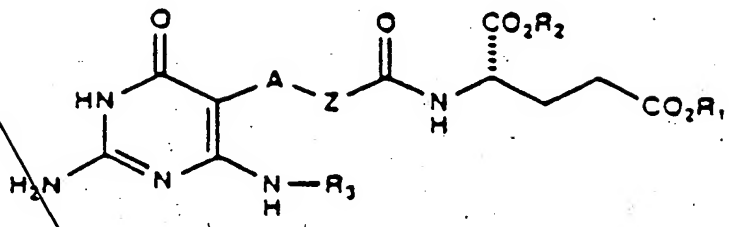
CLAIMS

1. A compound having the formula I



I

wherein:

A represents sulfur or selenium;

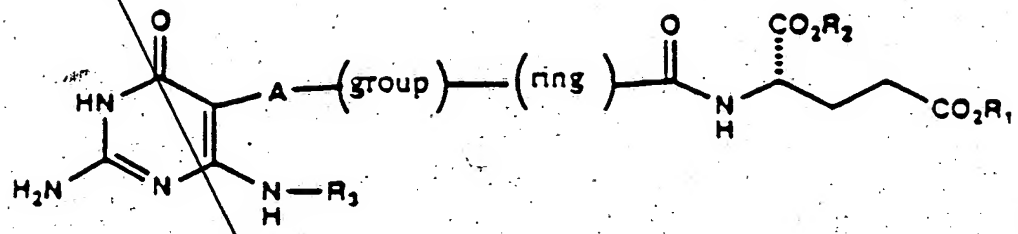
Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical, wherein when said non-cyclic spacer is bonded to A, said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms and further wherein when said non-cyclic spacer is bonded to -C(O)-, said non-cyclic spacer separates -C(O)- from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_1 and R_2 represent, independently, H or C_1 to C_6 alkyl or other readily lyzable groups; and

R_3 represents H or a straight, branched or cyclic C_1 to C_6 alkyl group optionally carrying one or more halogen, hydroxyl or amine groups; or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 having the formula

II



II

wherein:

A is sulfur or selenium;

Z is -(group)-(ring)-,

wherein (group) represents a non-cyclic spacer which separates A from (ring) by 1 to 5 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous and optionally carrying one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings;

and wherein (ring) represents one or more of a substituted or unsubstituted monocyclic carbo- or heterocyclic ring or a fused or non-fused polycarbocyclic or heterocyclic ring optionally substituted with one or more substituents selected from those recited for (group);

R_1 and R_2 represent, independently, H, C_1 to C_6 alkyl or other readily lyzable groups; and

R_3 represents hydrogen or a straight, branched or cyclic C_1 to C_6 alkyl group optionally carrying halogen, hydroxyl or amine substitution; or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1 wherein the moiety Z is represented by Q-X-Ar wherein:

Q represents a C_1-C_5 alkylene, or a C_2-C_5 alkenylene or alkynylene radical optionally carrying one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings;

X represents a methylene, monocyclic carbo- or heterocyclic ring, sulfur, oxygen or amino radical, optionally carrying one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings; and

Ar represents a monocyclic carbo- or heterocyclic aromatic ring or a bicyclic carbo- or heterocyclic ring, all or a portion of which may be aromatic, and wherein the Ar may be fused to the monocyclic carbo- or heterocyclic ring of X, and wherein the Ar optionally carries one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocycliccarbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings;

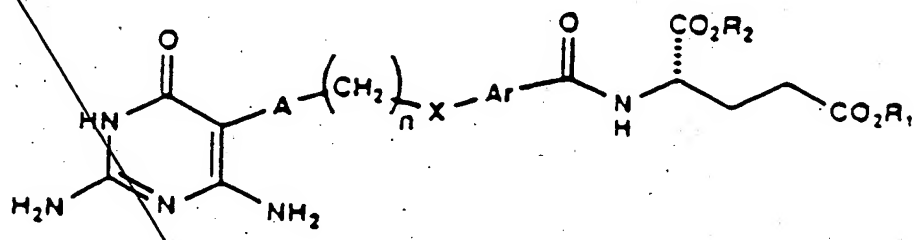
or a pharmaceutically acceptable salt thereof.

4. A compound or salt according to claim 2, wherein the moiety (group) represents a C_1 to C_4 alkylene group; and

the moiety (ring) represents a substituted or unsubstituted, fus d or non-fused carbocyclic or heterocyclic bicyclic ring system, or a substitut d or unsubstituted, carbocyclic or heterocyclic monocyclic ring system, or at

least two monocyclic ring systems linked by a single bond, said monocyclic ring systems being independently substituted or unsubstituted.

5. A compound having the formula III



III

wherein:

n represents an integer from 0 to 5;

A represents sulfur or selenium;

X is methylene, monocyclic carbo- or heterocyclic ring, O, S, or -NH-;

Ar is an aromatic radical, wherein Ar can form a fused bicyclic ring system with said ring of X; and

R_1 and R_2, which can be the same or different, are hydrogen or alkyl radicals having 1 to 6 carbon atoms;

or a pharmaceutically acceptable salt thereof.

6. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is methylene, Ar is phenylene and R_1 and R_2 are hydrogen.

7. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is methylene, Ar is 2,5-thienyl and R_1 and R_2 are hydrogen.

8. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is S, Ar is phenylene and R_1 and R_2 are hydrogen.

9. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is -NH-, Ar is phenylene and R_1 and R_2 are hydrogen.

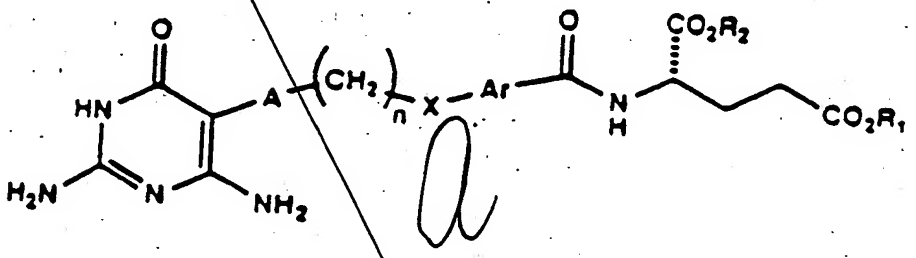
10. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is m thylene, Ar is phenylene and R_1 and R_2 are alkyl radicals having 1 to 6 carbon atoms.

11. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is methylene, Ar is 2,5-thienyl and R_1 and R_2 are ethyl groups.

12. A compound or salt according to claim 5 wherein n is 2, A is sulfur, X is sulfur, Ar is phenylene and R_1 and R_2 are ethyl groups.

13. A compound or salt according to claim 5, wherein n is 2, A is sulfur, X is -NH-, Ar is phenylene and R_1 and R_2 are ethyl groups.

14. An antiproliferative composition comprising a compound having the formula III



III

wherein n represents an integer from 0 to 5;

A is sulfur or selenium;

X is methylene, monocyclic carbo- or heterocyclic ring, O, S, or -NH-;

Ar is an aromatic radical, wherein Ar can form a fused bicyclic ring system with said ring of X; and

R_1 and R_2, which can be the same or different, are hydrogen or alkyl radicals having 1 to 6 carbon atoms; or

a pharmaceutically acceptable salt thereof

in combination with a pharmaceutically acceptable carrier.

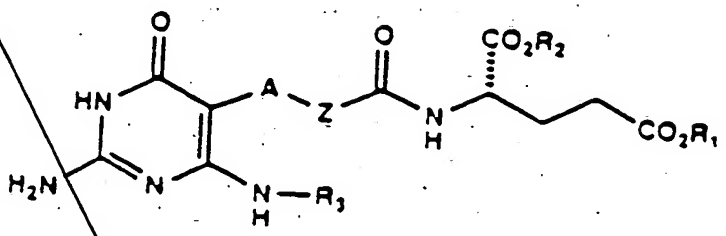
15. A composition according to claim 14 wherein n is 2, A is sulfur, X is methylene, and Ar is phenylene.

16. A composition according to claim 14 wherein n is 2, A is sulfur, X is methylene, and Ar is 2,5-thienyl.

17. A composition according to claim 14 wherein n is 2, A is sulfur, X is S, and Ar is phenylene.

18. A composition according to claim 14 wherein n is 2, A is sulfur, X is -NH-, and Ar is phenylene.

19. An antiproliferative composition comprising a compound having the formula I:



I

wherein:

A represents sulfur or selenium;

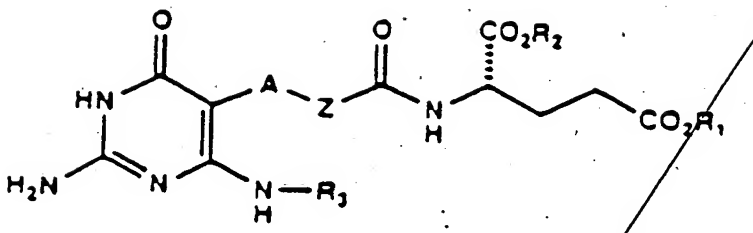
Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical, wherein when said non-cyclic spacer is bonded to A, said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms and further wherein when said non-cyclic spacer is bonded to -C(O)-, said non-cyclic spacer separates -C(O)- from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_1 and R_2 represent, independently, H, C_1 to C_6 alkyl or other readily lyzable groups; and

R_3 represents H or straight, branched or cyclic C_1 to C_6 alkyl group optionally carrying one or more halogen, hydroxyl or amine groups; or a pharmaceutically acceptable salt thereof;

in combination with a pharmaceutically acceptable carrier.

20. A process for inhibiting the growth and proliferation of the c lls of microorganisms and of higher organisms, which process comprises administering to a host in need of such treatment an effective amount of a compound having th structural formula I



I

wherein:

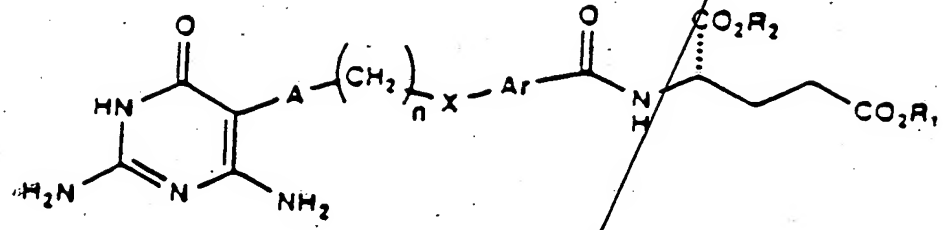
A represents sulfur or selenium;

Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical, wherein when said non-cyclic spacer is bonded to A, said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms and further wherein when said non-cyclic spacer is bonded to -C(O)-, said non-cyclic spacer separates -C(O)- from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_1 and R_2 represent, independently, H, C_1 to C_6 alkyl or other readily lyzable groups; and

R_3 represents H or straight, branched or cyclic C_1 to C_6 alkyl group optionally carrying one or more halogen, hydroxyl or amine groups; or a pharmaceutically acceptable salt thereof.

21. A process for inhibiting the growth and proliferation of the cells of microorganisms and higher organisms, which process comprises administering to a host in need of such treatment an effective amount of a compound having the structural formula III



III

wherein:

n represents an integer from 0 to 5;

A represents sulfur or selenium;

X is methylene, monocyclic carbo- or heterocyclic ring, O, S, or -NH-;

Ar is an aromatic radical, wherein Ar can form a fused bicyclic ring system with said ring of X; and

R_1 and R_2, which can be the same or different, are hydrogen or alkyl radicals having 1 to 6 carbon atoms; or

a pharmaceutically acceptable salt thereof.

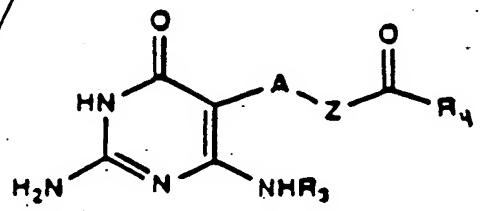
22. A process according to claim 21 wherein n is 2, A is sulfur, X is methylene and Ar is phenylene.

23. A process according to claim 21 wherein n is 2, A is sulfur, X is methylene and Ar is 2,5-thienyl.

24. A process according to claim 21 wherein n is 2, A is sulfur, X is sulfur and Ar is phenylene.

25. A process according to claim 21 wherein n is 2, A is sulfur, X is -NH-, and Ar is phenylene.

26. A process for preparing a 5-substituted pyrimidinone compound having the formula V



V

wher in:

A represents sulfur or selenium;

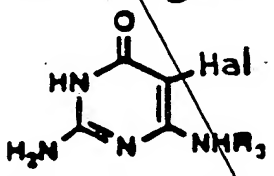
Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical, wherein said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_3 represents H or a straight, branched or cyclic (C_1 to C_6) alkyl group, optionally carrying one or more hydroxyl or amine groups; and

R_4 represents hydroxy, (C_1 to C_6) alkyloxy group optionally carrying one or more hydroxyl or amine groups, or a protected or unprotected amino acid linked to the acyl group of formula V by the amine portion of the amino acid;

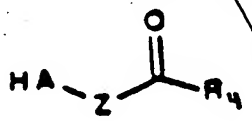
or a pharmaceutically acceptable salt thereof;

which process comprises reacting a compound having the formula VI



VI

wherein hal is bromine, chlorine, iodine, or fluorine, and R_3 is as defined above, with a compound having the formula IV



IV

wherein A, Z, and R_4 are as defined above, in the presence of a nonnucleophilic auxiliary base in a solvent in which at least one of said reactants is at least partially soluble under conditions sufficient to obtain the compound of formula V.

27. A process according to claim 26 wherein the non-nucleophilic auxiliary base is selected from alkali or earth metal carbonates and trialkyl amines.

28. A process according to claim 27 wherein the solvent is a dipolar aprotic solvent.

29. A process according to claim 28 wherein the solvent is selected from dimethylsulfoxide, N,N-dimethylformamide, N,N-dimethylacetamide, and N-methyl-2-pyrolidinone.

30. A process according to claim 26 wherein A represents sulfur and Z represents $-(CH_2)_n-X-Ar-$ wherein

n is an integer from 0 to 5,

X represents a methylene, monocyclic carbo- or heterocyclic ring, sulfur, oxygen or amino radical, optionally carrying one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings; and

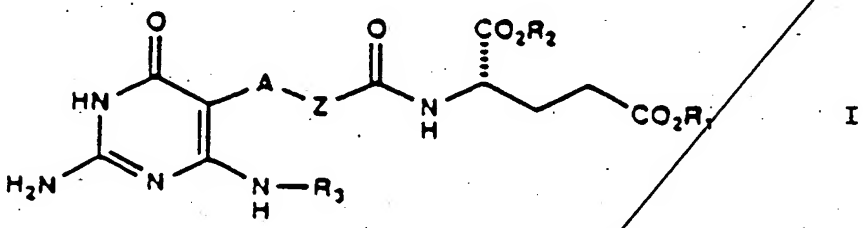
Ar represents a monocyclic carbo- or heterocyclic aromatic ring or a bicyclic carbo- or heterocyclic ring, all or a portion of which may be aromatic, and wherein the Ar may be fused to the monocyclic carbo- or heterocyclic ring of X, and wherein the Ar optionally carries one or more substituents independently selected from C_1 to C_6 alkyl or C_2 to C_6 alkenyl groups, C_1 to C_6 alkoxy or C_1 to C_6 alkoxy(C_1 to C_6)alkyl groups, C_2 to C_6 alkynyl groups, acyl groups, halogen, amino groups, hydroxyl groups, nitro groups or mercapto groups, monocyclic carbo- or heterocyclic rings, and fused or non-fused poly-carbocyclic or poly-heterocyclic rings.

31. A process according to claim 30 wherein the non-nucleophilic auxiliary base is selected from alkali or earth metal carbonates and trialkylamines.

32. A process according to claim 31 wherein the solvent is a dipolar aprotic solvent.

33. A process according to claim 32 wherein the solvent is selected from dimethylsulfoxide, N,N-dimethylformamide, N,N-dimethylacetamide, and N-m thyl-2-pyrolidinone.

34. A process for inhibiting GARFT comprising the step of administering to a host in need of such inhibition an effective amount of a compound having the formula I:



I

wherein:

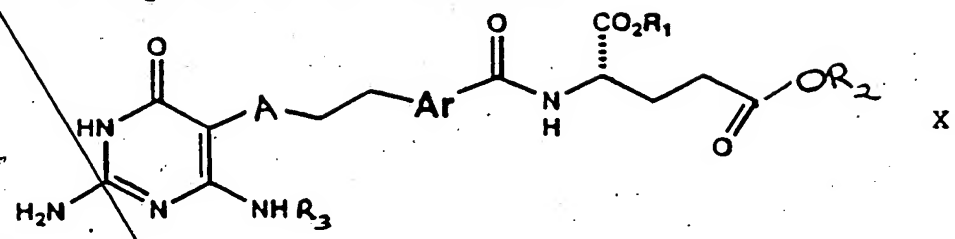
A represents sulfur or selenium;

Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least one of said non-cyclic spacer and at least one of said carbocyclic or heterocyclic radical, wherein when said non-cyclic spacer is bonded to A, said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms and further wherein when said non-cyclic spacer is bonded to -C(O)-, said non-cyclic spacer separates -C(O)- from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_1 and R_2 represent, independently, H or C_1 to C_6 alkyl or other readily lyzable groups; and

R_3 represents H or straight, branched or cyclic C_1 to C_6 alkyl group optionally carrying one or more halogen, hydroxyl or amine groups; or a pharmaceutically acceptable salt thereof.

35. A compound of the formula X



wherein:

A represents sulfur or selenium;

Ar represents an unsubstituted phenylene or thienylene radical;

R_1 and R_2 represent, individually, hydrogen or C_1 to C_6 alkyl or other readily lyzable groups;

R_3 represents hydrogen or a straight, branched or cyclic C_1-C_6 alkyl group, optionally carrying one or more halogen, hydroxyl or amine groups; or

a pharmaceutically acceptable salt thereof.

36. A compound according to claim 35 wherein A is sulfur and Ar represents an unsubstituted phenylene radical.

37. A compound according to claim 35 wherein A is sulfur and Ar represents an unsubstituted thienylene radical.

38. A compound according to claim 35 wherein A is sulfur, Ar is unsubstituted thienylene; and R_1, R_2 and R_3 are hydrogen.

39. A compound according to claim 35 wherein A is sulfur, Ar is unsubstituted phenylene; and R_1, R_2 and R_3 are hydrogen.

40. A method for inhibiting the growth and proliferation of the cells of microorganisms and higher organisms, which comprises administering to a host in need of such treatment an effective amount of the compound having th structural formula X as defined in claim 35, or a pharmaceutically acceptable salt thereof.

41. A method according to claim 40 wherein A is sulfur and Ar repr s nts an unsubstituted phenyl ne radical.

42. A method according to claim 40 wherein A is sulfur and Ar repres nts an unsubstitut d thi nylen radical.

43. A method according to claim 40 wherein A is sulfur, Ar is an unsubstituted thienylene radical; and R_1, R_2 and R_3 are hydrogen.

44. A method according to claim 40 wherein A is sulfur, Ar is an unsubstituted phenylene radical; and R_1, R_2 and R_3 are hydrogen.

45. An antiproliferative composition comprising the compound having the formula X as defined in claim 35 or a pharamaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

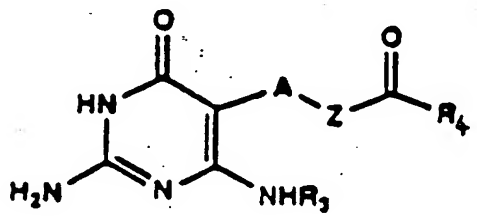
46. A composition according to claim 45 wherein A is sulfur and Ar represents an unsubstituted phenylene radical.

47. A composition according to claim 45 wherein A is sulfur and Ar represents an unsubstitued thienylene radical.

48. A composition according to claim 45 wherein A is sulfur, Ar is an unsubstituted thienylene radical; and R_1, R_2 and R_3 are hydrogen.

49. A composition according to claim 45 wherein A is sulfur, Ar is an unsubstituted phenylene; and R_1, R_2 and R_3 are hydrogen.

50. A compound having the formula V



V

wherein:

A represents sulfur or selenium;

Z represents 1) a substituted or unsubstituted non-cyclic spacer which separates A from the carbonyl carbon of the amido group by 1 to 10 atoms, said atoms being independently selected from carbon, oxygen, sulfur, nitrogen and phosphorous; 2) a substituted or unsubstituted mono- or fused or nonfused poly-carbocyclic or heterocyclic radical; or 3) a combination of at least on of said non-cyclic spacer and at least on of said carbocyclic or heterocyclic radical,

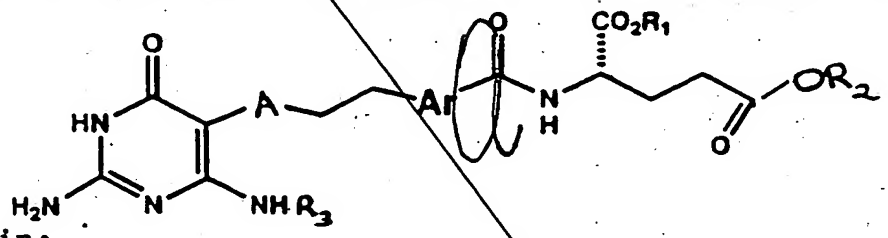
wher in said non-cyclic spacer separates A from one of said carbocyclic or heterocyclic radicals by 1 to 10 atoms;

R_3 represents H or a straight, branched or cyclic (C_1 to C_6) alkyl group, optionally carrying one or more hydroxyl or amine groups; and

R_4 represents hydroxy, (C_1 to C_6) alkyloxy group optionally carrying one or more hydroxyl or amine groups, or a protected or unprotected amino acid linked to the acyl group of formula V by the amine portion of the amino acid;

or a pharmaceutically acceptable salt thereof.

51. A process for inhibiting AICARFT comprising the step of administering to a host in need of such inhibition an effective amount of a compound having the formula X:



X

wherein:

A represents sulfur or selenium;

Ar represents an unsubstituted phenylene or thienylene radical;

R_1 and R_2 represent, individually, hydrogen or C_1 to C_6 alkyl or other readily lyzable groups;

R_3 represents hydrogen or a straight, branched or cyclic C_1-C_6 alkyl group, optionally carrying one or more halogen, hydroxyl or amine groups; or

a pharmaceutically acceptable salt thereof.

add A²

add C¹